EARLY ONSET OF OCULAR AUTOIMMUNE MYASTHENIA – CASE REPORT

Raluca Ioana Teleanu[1,2], Smaranda Nita[2], Daniela Vasile[2]

[1]"Carol Davila" University of Medicine and Pharmacy, Bucharest

[2]"Dr. Victor Gomoiu" Children's Hospital, Department of Pediatric Neurology, Bucharest

ABSTRACT

The article aims to present a rare case of autoimmune myasthenia diagnosed in our clinic with an onset before the age of threein a girl initially presentingblepharoptosis, exotropia and nystagmus. The exclusive ocular involvement has persisted throughout the clinical course of eleven months until the present moment, showing partial improvement under daily administration of pyridostigmine bromide. Finally we wish to underline the future possible outcomes and management options which were taken into consideration in this case, as well as to emphasize the positive role of a multidisciplinary approach in assessing pediatric patients.

Key words: myasthenia gravis, autoimmune, ocular, early onset, child

INTRODUCTION

Myasthenia gravis is a chronic disease characterized by rapid fatigability of striated muscles. There are three main clinical forms affecting children: juvenile myasthenia gravis, congenital myasthenia and transient neonatal myasthenia. Also, a postinfectious transitory myasthenia gravis can follow a varicella-zoster infection.

The most common cause is an autoimmune-mediated blockade of the acetylcholine receptors (AchR), with accompanying elevated anti – AchR antibodies, which are thought to be produced through T-cell activation (1). However, these antibodies can only occasionally be found in the plasma of prepubertal children (2). A variety of mostly autosomal recessive familial forms are not associated with plasma anti – AchR antibodies. In these cases, plasmatic anti – muscle specific tyrosine kinase (MuSK) antibodies can be elevated.

Infants born to myasthenic mothers can develop a transient neonatal myasthenic syndrome associated to anti AchR antibodies transferred via the placenta.

Clinically, myasthenia gravis is divided, according to the Myasthenia Gravis Foundation of America Clinical Classification (3), into five main classes and several subclasses, the first class designating the pure ocular forms, involving solely the extraocular muscles, while the others describe different patterns of systemic involvement, also affecting other different muscle groups: facial, swallowing, respiratory, limbs.

The diagnosis of myasthenia gravis is based on the clinical aspect of progressive diurnal muscle fatigability and various paraclinical examinations. In the autoimmune type of myasthenia, the presence of anti – AchR antibodies is diagnostic. However, a large proportion of patients are seronegative and they are sometimes likely to demonstrate elevated anti – MuSK antibodies.An anticholinesterase test is helpful, as it is also likely to predict a response to longer –acting acetylcholine esterase inhibitors[7]. The test is performed by assessing the clinical muscle weakness before and after administration of a short – acting acetylcholine esterase inhibitor, typically edrophonium. Electrodiagnostic studies,

Author for correspondence:
Assoc. Prof. Raluca IoanaTeleanu MD, PhD, "Dr. Victor Gomoiu" Children's Hospital, Basarabia Bd. 21, Bucharest, Romania
e-mail: ralucate@gmail.com

namely repetitive nerve stimulation (RNS) and single-fiber electromyography (SFEMG), are of importance in myasthenia gravis, as they can demonstrate a defective neuromuscular transmission. While SFEMG is more sensitive than RNS, it is also more difficult to perform in children.Ancillary testing includes thoracic computer tomography of magnetic resonance imaging (MRI) to investigate the possibility of thymus hyperplasia. Also, a cerebral imagistic examination should be performed in order to rule out lesions compressing the cranial nerves in ocular myasthenia.

Although there are is no clear consensus in the treatment of myasthenia gravis, therapeutic options consist of: acetylcholine esterase inhibitors, thymectomy, corticosteroids and other immunosuppresive agents such as azathioprine, cyclosporine A, mycophenolate mofetil, rituximab, depending on the degree of muscle involvement and severity of the disease. Intravenous immunoglobulin and plasmapheresis are reserved for refractory cases.

In this article we present a case of early onset autoimmune – mediated myasthenic syndrome, with ocular involvement.

CASE REPORT

A two year and eight month oldgirl with no perinatal events and normal development (as well as a negative family history for neuromuscular or autoimmune pathology) was brought to our clinic for sudden onset of bilateral asymmetric blepharoptosis (Fig. 1), bilateral exotropia and diplopia with occasional laterocollis. These simptoms had a variable course and fluctuation throughout the day and partial remission with sleep. In addition there was no history of swallowing difficulties, dyspnea, other associated muscle weakness or gait disturbance. The neurological examination revealed the signs mentioned above, as well as gaze – evoked nystagmus. Her physical examination was otherwise normal.

An ophthalmologic evaluation was carried out and was within normal limits. The cerebral magnetic resonance imaging (MRI) ruled out any central nervous system involvement.

The blood testing was normal and the inflammatory markers were negative. Cardiac as well as abdominal ultrasound revealed no abnormalities.

Upon suspicion of myathenia gravis, the electromyographic studies could not be carried out due to poor colaboration with the child and were delayed for further evaluation. However, an anticholinesterase test was performed using subcutaneous

FIGURE 1. *Blepharoptosis*

administration of 0,5 mg of neostigmine which revealed a delayed response.

Subsequently, the plasmatic levels of anti – AchR antibodies were found to be highly elevated (33 nmol/L with normal values at less than 0,2 nmol/L). There was no elevation of anti- MuSK antibodies or associated thyroid autoimmune pathology as assessed by measurement of thyroid – specific antibodies and endocrinological examination.

Consequently, the diagnosis was of autoimmune – mediated ocular myasthenia and the patient was started on pyridostigmine bromide at 7 mg/Kg/day, five times/day, daytime only, with visible and video – documented partial improvement and no additional muscle involvement. Her condition has persisted throughout the course of eleven months, until the present moment. Also, on further evaluation, a cardio – thoracic MRI revealed no thymus hyperplasia.

Prognosis and future therapeutic options

Given the relatively constant clinical course under pyridostigmine bromide, a further step in trying to achieve possible remission is thymectomy around the age of five years, despite lack of thymus hyperplasia, considering the presumed role of the thymus in the pathogeny of the disease (4).

Corticoid and immunosuppresive therapies are not considered an option at this time, upon balancing the adverse effects (5) and the ocular form of the disease.

In this case, future progress towards a systemic form is of concern, in which case the above mentioned therapeutic alternatives should be considered. On the other hand, at prepubertal age of onset, there is evidence that systemic involvement is less often encountered (6).

The child will continue to be monitored with the aid of a multidisciplinary team comprised of a pediatric neurologist, a pediatrician and anophtalmologist.

CONCLUSIONS

We have presented a rare case of autoimmune myasthenia with exclusive ocular involvement, starting at an early age. Because of exclusive ocular involvement, often the first evaluation that such a child undergoesis ophthalmologic. Therefore, myasthenia must be taken into consideration by ophthalmologists and cooperation with the pediatric neurologist is needed.

With respect to the case presented, daily administration of pyridostigmine bromide has proven useful up to this point while thymectomy is taken into consideration for future management.

REFERENCES

1. **Sakuma H., Katayama A., Saito Y., etc.** – CD4+CD25 high regulatory T cell in childhood ocularmyasthenia gravis, *Brain& Development*, 2011; 33(5):442-4
2. **Finnis M.F., Jayawant S.** – Juvenile Myasthenia Gravis: A Paediatric Perspective, *Autoimmune Diseases*, 2011; Volume 2011: Article ID 404101, 7 pages
3. **Jaretzki A., Barohn R.J., Ernstoff R.M., etc.** – Myasthenia Gravis: Recommendations for Clinical Research Standards, *Neurology*, 2000; Volume 55, No 1
4. **Ware T.L., Ryan M.M., Kornberg A.J.** – Autoimmune myasthenia gravis, immunotherapy and thymectomy in children, *Neuromuscular Disorders,* 2012; 22(2):118-21
5. **Ishigaki K., Shishikura K., Murakami T.** – Benefits of FK 506 for refractory eye symptoms in a young child with ocular myasthenia gravis, *Brain & Development,* 2008; 31(8):634-7
6. **Peneles S.L., Avery R.A., Moss H.E., etc.** – Visual and Systemic Outcomes in Pediatric Ocular Myasthenia Gravis, *American Journal of Ophthalmology*, 2010; Volume 150, Issue 4, 453-459
7. **Ionita C.M., Acsadi G.** – "Management of Juvenile Myasthenia Gravis", *Pediatric Neurology*, 2012; 48, 95-104